08/875888

FORM PTO-1390 (Rev. 11-92) — U.S. Department of Commerce Patent and Trademark Office

TRANSMITTAL LETTER OF THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US)

Attorney's Docket Number: ABA300/13003

International Application No.	International Filing Date	Priority Dates Claimed
PCT/SE97/00566	1 April 1997	12 April 1996

Title of Invention: New Pharmaceutical Composition with Anaesthetic Effect

Applicant(s) for DO/EO/US: Arne Brodin, Raymond Fynes, Lars Heijl, Adela Nyqvist-Mayer and Marie Scherlund

Applicant herewith submits to the United States Designed/Elected Office (DO/EO/US) the following items under 35 U.S.C. 371:

1. ☐ This express request to immediately begin national examination procedures (35 U.S.C. 371(f)).
2. ☒ The U.S. National Fee (35 U.S.C. 371(c)(1)) and other fees as follows:

CLAIMS	(1) FOR	(2) NUMBER FILED	(3) NUMBER EXTRA	(4) RATE	(5) CALCULATIONS
	TOTAL CLAIMS	20-20 =	0	44 X $22.00	$ -0-
	INDEPENDENT CLAIMS	3-3 =	0	0 X $80.00	-0-
	MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ $260.00	260.00
	Basic National Fee (37 CFR 1.492(a)(1)-(5)):				
	☐ For filing with EPO or JPO search report (37 CFR 1.492(a)(5)) . . . $910.00				
	☐ International preliminary examination fee paid to USPTO (37 CFR 1.482) $700.00				
	☐ No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2)) $770.00				
	☒ Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO $1,040.00				1,040.00
	☐ International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Articles 33(2)-33(4) $96.00				
	Surcharge of **$130.00** for furnishing the National fee or oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(e)).				
			TOTAL OF ABOVE CALCULATIONS	=	1,300.00
	Reduction by 1/2 for filing by small entity, if applicable. Affidavit must be filed also. (Note 37 CFR 1.9, 1.27, 1.28).				
			SUBTOTAL	+	1,300.00
	Processing fee of $130.00 for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(f)).				
			TOTAL NATIONAL FEE	$	1,300.00
	Fee for recording the enclosed assignment (37 CFR 1.21(h)).			+	40.00
			TOTAL FEES ENCLOSED	$	1,340.00

a. ☒ Checks in the amounts of $1,300.00 and $40.00 to cover the above fees are enclosed.

b. ☐ Please charge my Deposit Account No. 22-0365 in the amount of $_____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 22-0365. A duplicate copy of this sheet is enclosed.

Attorney's Docket Number
ABA300/13003

3. A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. ☒ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
   c. ☐ has been transmitted by the International Bureau.

4. ☐ A translation of the International Application into English (35 U.S.C. 371(c)(2)).

5. Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ have been transmitted by the International Bureau.

6. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).

7. ☒ An oath or declaration of the inventors (35 U.S.C. 371(c)(4)).

8. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. § 371(c)(5)).

9. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.

10. ☒ An assignment document for recording.
    PLEASE MAIL THE RECORDED ASSIGNMENT DOCUMENT TO:
    a. ☐ the person whose signature, name and address appears at the bottom of the page.
    b. ☒ the following: Robert A. Armitage
    Vinson & Elkins L.L.P.
    The Willard Office Building
    1455 Pennsylvania Ave. N.W., Suite 800
    Washington, D.C. 20004-1008

11. The above checked items are being transmitted:
    a. ☒ before the eighteenth (18th) month publication.
    b. ☐ after publication of the Article 20 communication but before twenty (20) months from the priority date.
    c. ☐ after twenty (20) months but before twenty-two (22) months (surcharge and/or processing fee included).
    d. ☐ after twenty-two (22) months (surcharge and/or processing fee included).
    e. ☐ by thirty (30) months and a proper demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
    f. ☐ after thirty (30) months but before thirty-two (32) months and a proper demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date (surcharge and/or processing fee included).
    g. ☐ after thirty-two (32) months (surcharge and/or processing fee included).

12. At the time of transmittal, the time limit for amending claims under Article 19:
    a. ☐ has expired and no amendments were made.
    b. ☒ has not yet expired.

13. ☐ Certain requirements under 35 U.S.C. 371 were previously submitted by the applicant on _____, namely:

14. ☒ Applicants do not request expedited handling of this application and do not request that the National Stage of processing be commenced prior to the expiration of the applicable time limits under Article 22(1) or (2), or under Article 39(1)(a) of the PCT. 35 U.S.C. 371(f).

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August 6, 1997

The Assistant Commissioner for Patents
Washington, DC 20231

Box: Patent Application

Re: Entry into National Stage for:
Intl. Appl. No.: PCT/SE97/00566
Intl. Filing Date: 1 April 1997
For: **New Pharmaceutical Composition With Anaesthetic Effect**
Inventor(s): Brodin *et al.*
Our Ref.: ABA300/13003

Sir:

The following documents are being forwarded herewith for appropriate action by the U.S. Patent and Trademark Office:

1. Form PTO-1390, Transmittal Letter of the United States Designated/Elected Office (2 pages);

2. A copy of application PCT/SE97/00566 as filed in the PCT Receiving Office in Sweden on April 1, 1997 and comprising:

   a title page naming Arne Brodin, Raymond Fynes, Lars Heijl, Adela Nyqvist-Mayer and Marie Scherlund as inventors (unnumbered)
   12 pages of specification (numbered as pages 1-12)
   4 pages of claims (numbered as pages 13-16) and
   a one page abstract (numbered as page 17);

3. Combined Declaration and Power of Attorney executed by inventors Arne Brodin, Raymond Fynes, Lars Heijl, Adela Nyqvist-Mayer and Marie Scherlund (4 pages);

4. Assignment to Astra AB executed by inventors Arne Brodin, Raymond Fynes, Lars Heijl, Adela Nyqvist-Mayer and Marie Scherlund (2 pages), the recordation of which is respectfully requested;

5. Form PTO-1594, Recordation Form Cover Sheet;

6. Our check no. 112794 in the amount of $1,300.00 covering the filing fees for this matter, and our check no. 112793 in the amount of $40.00 covering the fee for recordation of the Assignment; and

7. Two (2) return postcards.

Applicants are submitting the enclosed documents for the purpose of entering into the National Stage for the above-captioned PCT application. Applicants are *not* requesting expedited handling of this application and do *not* request that the National Stage of processing be commenced prior to the expiration of the applicable time limits under Article 22(1) or (2), or under Article 39(1)(a) of the PCT.

It is respectfully requested that the enclosed postpaid post card be stamped with the date the enclosed documents are received by the PTO and that it be returned as soon as possible.

The Commissioner is hereby authorized to charge any fee deficiency or credit any overpayment to our Deposit Account No. 22-0365. A duplicate copy of this letter is enclosed.

Respectfully requested,

VINSON & ELKINS L.L.P.

Michael A. Sanzo

Michael A. Sanzo
Attorney for Applicants
Registration No. 36,912

MAS:ct
Attachments

ASTRA

Applicant: **Astra Aktiebolag**
S-151 85 Södertälje
Sweden

Title: **NEW PHARMACEUTICAL COMPOSITION WITH ANAESTHETIC EFFECT**

Reference: P 1550-1

Inventors: Arne Brodin
Raymond Fynes
Lars Heijl
Adela Nyqvist-Mayer
Marie Scherlund

NEW PHARMACEUTICAL COMPOSITION WITH ANAESTHETIC EFFECT

The field of the invention

The present invention is directed to a new pharmaceutical composition and its use in therapy, particularly as an anaesthetic for use on mucous membranes and particularly within the oral cavity.

Background and prior art

It is estimated that approximately 10-13 % of the population suffers from periodontal diseases with pathological periodontal pockets. In order to eliminate or control the disease and arrest further periodontal tissue destruction, periodontal pockets need repeated subgingival mechanical debridement/cleansing. The number of periodontal pockets in a patient may vary as can the pocket depth measurement. Approximately 40 % of all periodontal scaling procedures performed involve some kind of anaesthesia.

Accumulation of bacterial plaque on teeth and in the gingival sulcus elicits an inflammatory response in the marginal gingiva which may spread in an apical direction and result in loss of tooth support with the formation of periodontal pockets. The object of mechanical debridement of periodontal pockets is to control and arrest further destruction of tooth support by removal of plaque and calculus from within the pockets.

The majority of the scaling procedures are performed by hygienists. The main use of anaesthesia techniques used in conjunction with periodontal scaling is either a nerve block or infiltration. Infiltration anaesthesia is either carried out alone or in combination with topical anaesthesia, mainly jelly, ointment or spray. However, the problem with existing topical products are lack of efficacy due to inadequate depth of penetration, too short duration and difficulties in administration due to spread, taste etc.

EP 244 118 discloses a controlled release drug delivery system for placement in the periodontal pocket, having a plurality of discrete microparticles consisting of a rate-controlling polymer matrix having a drug dispersed therein, said microparticles being in the range of 10-500 μm. EP 241 178 also discloses a controlled release drug delivery system for placement in the periodontal pocket, which composition comprises solid particles having an average size of 1-500 μm. However, the drug delivery systems disclosed in both these prior art patents are deviced for administration of a medicament for a longer period of time. Thus the drug delivery systems of EP 244 118 and EP 241 178 are not suitable for use in pain management in conjunction with minor surgical procedures, where a fast onset of action and relatively short duration is required.

Thus, the problem underlying the present invention is to provide a pharmaceutical composition which would provide effective pain relief in conjunction with periodontal scaling and root planing following local administration. In other words, the object of the invention is to provide a local anaesthetic that can be applied in a facile manner in the oral cavity, and more precisely within periodontal pockets. A further object of the invention is to provide a pharmaceutical composition having a short onset time and an adequate duration for the intended procedure, with no inconvenient anaesthesia.

Outline of the invention

The problem identified above has now been solved by providing a new pharmaceutical composition which preferably is in form of an emulsion, more preferably in form of a microemulsion, comprising the following ingredients:

(i) One or more local anaesthetics in oil form in the final composition;

(ii) one or more surfactants, together present in an amount effective to produce a homogenous formulation; and

(iii) water up to 100 % by weight, based on the total weight of the composition.

The local anaesthetic in the final composition is one or more local anaesthetics in oil form as such, or a eutectic mixture formed by two or more local anaesthetics. The amount of the local anaesthetic in the oil phase depends on the pH-value of the formulation.

In a particularly preferred embodiment of the invention the local anaesthetic is a eutectic mixture of lidocaine base and prilocaine base.

In a further embodiment of the invention a eutectic mixture may also be formed by two or more substances, where at least one of these substances is a local anaesthetic.

The amount of the local anaesthetic or mixture of local anaesthetics is preferably in the range 0.5 - 20 % by weight, more preferably in the range 2-7 % by weight, based on the total weight of the composition.

The local anaesthetic(s) in the final composition are present in a non-solid form.

By the wording "surfactant" we mean any agent that acts as a solubilizer and/or as an emulsifier and/or as a thickening agent with thermoreversible gelling properties. The wording surfactant is also intended to include thickening agents without thermoreversible properties. If only one surfactant is used in the composition, it must be selected with care and in suitable amounts so that it acts both as a solubilizer and/or as an emulsifier, as well as a thickening agent with thermoreversible gelling properties. If more than one surfactant is present in the composition, at least one of the surfactants should have thermoreversible gelling properties. The total amount of the surfactant(s) should be present in an amount effective to produce a homogenous formulation.

The surfactants are preferably selected from non-ionic surfactants, more preferably from any non-ionic poloxamer known in the art.

Poloxamers are synthetic block copolymers of hydrophilic ethylene oxide chains and hydrophobic propylene oxide chains, having the general formula $HO\text{-}[C_2H_4O]_a\text{-}[C_3H_6O]_b\text{-}[C_2H_4O]_a\text{-}H$, a and b representing the number of the hydrophilic and hydrophobic chains respectively.

By choosing the surfactant(s) having hydrophobic and hydrophilic domains in appropriate amounts, in combination with an appropriate amount of the local anaesthetic or mixture of local anaesthetics, it is possible to achieve a composition having suitable thermoreversible gelling properties, i.e. the system remains less viscous at room temperature, and upon application into a periodontal pocket the viscosity of the composition is increased. In other words, the pharmaceutical composition according to the present invention is less viscous at room temperature. Above this temperature the composition is more viscous, providing the advantage of remaining in the periodontal pockets for the time necessary to induce local anaesthesia. The change in viscosity is reversible with temperature.

In a particularly preferred embodiment of the invention the surfactant is one or more of Lutrol F68®, which also has the name poloxamer 188 and wherein a= 80 and b=27, and Lutrol F127®, which also has the name poloxamer 407 and wherein a=101 and b=56, the definitions being in accordance with USP (1995) NF18, p. 2279. Lutrol F68® and Lutrol F127® are commercially available from BASF.

In a further preferred embodiment of the invention the surfactant Arlatone 289® is used, which also has the name polyoxyethylene hydrogenated castor oil, as well as Adinol CT95® which is sodium N-methyl N-cocoyl taurate.

The total amount of surfactant(s) is preferably present in an amount of up to 50 % by weight, based on the total weight of the composition.

The pH-value of the pharmaceutical composition is adjusted with suitable acid or base in such a way that the final pH-value for the composition is:

(A) $pH \geq [pK_a$ (local anaesthetic) - 1.0] if the composition comprises one local anaesthetic; or

(B) $pH \geq [pK_a$ (local anaesthetic with the lowest pK_a value) - 1.0] if the composition comprises two or more local anaesthetics.

Preferably the pH is over 7.5.

Since local anaesthetics by nature have an unpleasant bitter taste, one or more taste masking agents may optionally be added to the pharmaceutical composition. The choice of taste masking agents will be appreciated by a person skilled in the art, but as an example any fruit flavours may be mentioned.

By topical application within the periodontal pocket, local anaesthesia is achieved in a very localised area, without causing the often extensive soft tissues such as the tongue, cheek and lips, to get anaesthetized which is often the case with infiltration anaesthesia. Preferably the composition is applied into a periodontal pocket by means of a blunt needle, thereby facilitating the administration of the anaesthetic and giving an increased patient comfort.

The pharmaceutical composition of the present invention has a fast onset of action being from seconds and up to approximately 5-15 minutes. The onset time is most preferably from seconds and up to approximately 5 minutes.

For the definition of emulsions, we refer to *Pharmaceutics, The Science of Dosage Form Design, 1988, p. 109-110, by ME Aulton.*

The pharmaceutical composition according to the present invention is preferably a microemulsion. By microemulsion we mean a formulation that consists of water, oil and amphiphile(s) which constitute a single optically isotropic and thermodynamically stable liquid solution (*I. Danielsson and B Lindman, Colloids Surf. 3:391, (1981)*).
This provides a suitable amount of the local anaesthetic in the oil phase, which in turn confers a fast onset of action. No separate oil needs to be added to the composition, since the oil is already present by the active component(s) as such. A further advantage is that a thermodynamically stable composition is achieved in a temperature range of 5-40 °C.

The pharmaceutical composition according to the present invention may advantageously also be used as a local anaesthetic on other surfaces and/or cavities than in the oral cavity. The composition may thus also be used vaginally, genitally and rectally.

The local anaesthetic(s) used for preparing a pharmaceutical composition according to the present invention may be selected from any local anaesthetic. Preferably the local anaesthetic as the starting material is in a non-ionized form.

In the final composition a fraction of the local anaesthetic or mixture of local anaesthetics are present in oil form. The size of this fraction, local anaesthetics in oil form, depends on the pH of the composition.

The best mode of performing the invention known at present, is to use the composition according to Example 1.

Methods of preparation

The pharmaceutical composition according to the present invention may be prepared by the following steps:

(i) the local anaesthetic(s) and the surfactant with the lowest molecular weight if more than one surfactant is used, are melted together;

(ii) a part of the water is slowly added to the melt (i) during homogenization, forming an emulsion concentrate;

(iii) if more than one surfactant is used, the surfactant with the higher molecular weight is dispersed in water;

(iv) the emulsion concentrate of step (ii) and part of the surfactant solution of step (iii) are thoroughly mixed;

(v) the pH-value is adjusted by the addition of a suitable acid or base;

(vi) the weight is adjusted with water to the final weight of the composition.

The composition is preferably kept at 5 °C until a homogenous composition is obtained.

Detailed description of the invention

The invention will now be described in more detail by the following examples, which are not to be construed as limiting the invention.

Example 1	[% by weight]
Lidocaine	2.50
Prilocaine	2.50
Lutrol F68®	5.50
Lutrol F127®	15.50

purified water up to a total weight of 100 %.

The composition was prepared by following the procedure described above, and the pH-value was adjusted by adding 2 M hydrochloric acid.

Example 2	[% by weight]
Lidocaine	2.50
Prilocaine	2.50
Lutrol F68®	5.00
Lutrol F127®	16.25

purified water up to a total weight of 100 %.

The composition was prepared by following the procedure described above, and the pH-value was adjusted by adding 2 M hydrochloric acid.

Example 3	[% by weight]
Lidocaine	2.25
Prilocaine	2.25
Lutrol F68®	3.5
Lutrol F127®	14.0

purified water up to a total weight of 100 %.

The composition was prepared by following the procedure described above, and the pH-value was adjusted by adding 2 M hydrochloric acid.

Example 4	[% by weight]
Lidocaine	2.25
Prilocaine	2.25
Arlatone 289®	1.90
Adinol CT95®	0.07
Lutrol F127	14.00

purified water up to a total weight of 100 %.

The composition was prepared by following the procedure described above, and the pH-value was adjusted by adding 2 M hydrochloric acid.

Example 5	[% by weight]
Lidocaine	2.25
Prilocaine	2.25
Arlatone 289®	1.90
Adinol CT95®	0.16
Lutrol F127	14.00

purified water up to a total weight of 100 %.

The composition was prepared by following the procedure described above, and the pH-value was adjusted by adding 2 M hydrochloric acid.

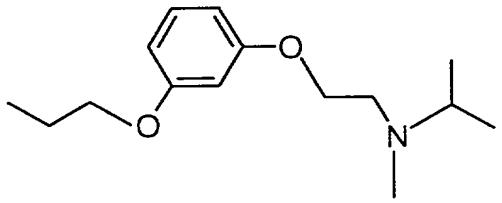
Example 6	[% by weight]
Lidocaine	2.25
Prilocaine	2.25
Arlatone 289®	1.90
Adinol CT95®	0.28
Lutrol F127	14.00

purified water up to a total weight of 100 %.

The composition was prepared by following the procedure described above, and the pH-value was adjusted by adding 2 M hydrochloric acid.

Example 7 and 8

In Examples 7 and 8, a local anaesthetic of the formula (I) was used as the acive ingredient.



(I)

This compound is disclosed in the International Patent Application SE96/01361.

The following pharmaceutical compositions were prepared.

Example 7	[% by weight]
Compound (I)	2.5
Lutrol F127®	17.0
Lutrol F68®	5.5

purified water up to a total weight of 100 %.

The composition was prepared by following the procedure described above, and the pH-value was adjusted by adding 2 M hydrochloric acid.

Example 8	[% by weight]
Compound (I)	2.5
Lutrol F127®	20.0
Lutrol F68®	5.5

purified water up to a total weight of 100 %.

The composition was prepared by following the procedure described above, and the pH-value was adjusted by adding 2 M hydrochloric acid.

Biological studies

A pharmaceutical composition according to Example 1 was applied to a human periodontal pocket with a blunt end needle. After an onset time of 30 - 45 seconds, a satisfactory anaesthetic effect had been achieved in order that periodontal scaling could be performed. The scaling was initiated, and the time taken to scale the toth was noted. At the end of the scaling, the intensity of pain was measured by means of a visual analogue scale (VAS). The duration of the anaesthetic effect was 10-20 minutes.

Claims

1. A pharmaceutical composition comprising

(i) one or more local anaesthetics in oil form in the final composition;

(ii) one or more surfactants, together present in an amount effective to produce a homogenous formulation; and

(iii) water up to 100 % by weight, based on the total weight of the composition.

2. A pharmaceutical composition according to claim 1, further comprising one or more taste masking agents.

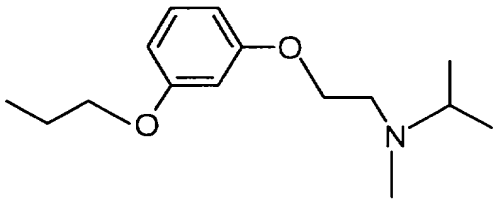
3. A pharmaceutical composition according to claim 1 or 2, wherein the amount of the local anaesthetic or mixture of local anaesthetics is present in an amount of 0.5 - 20 % by weight based on the total weight of the composition.

4. A pharmaceutical composition according to claim 3, wherein the amount of local anaesthetic or mixture of local anaesthetics being present in an amount of 2-7 % by weight based on the total weight of the composition.

5. A pharmaceutical composition according to any of the preceding claims, wherein the active ingredient is a eutectic mixture of local anaesthetics.

6. A pharmaceutical composition according to claim 5, wherein the active ingredient is a eutectic mixture of lidocaine and prilocaine.

7. A pharmaceutical composition according to claim 1, wherein the active ingredient is



(I)

8. A pharmaceutical composition according to any of the preceding claims, comprising more than one surfactant of which at least one is a surfactant having thermoreversible gelling properties.

9. A pharmaceutical composition according to any of the preceding claims, the total amount of the surfactant(s) being present in an amount of up to 50 % by weight based on the total weight of the composition.

10. A pharmaceutical composition according to any of the preceding claims, wherein the surfactant is a non-ionic surfactant.

11. A pharmaceutical composition according to claim 10, wherein the surfactant is a poloxamer.

12. A pharmaceutical composition according to any of the preceding claims, comprising the two surfactants Lutrol F68® and Lutrol F127® .

13. A pharmaceutical composition according to any of the preceding claims for use in therapy.

14. A pharmaceutical composition according to claim 13, for use as a local anaesthetic administered on the mucosa of the oral cavity.

15. A pharmaceutical composition according to claim 14, the therapeutic indication being pain relief during periodontal scaling.

16. Use of a pharmaceutical composition according to claim 1, for the manufacture of a medicament for pain relief during periodontal scaling.

17. A method for the treatment of pain associated with periodontal scaling, whereby a pharmaceutical composition according to claim 1 is applied to a patient in the need of pain relief during periodontal scaling.

18. A process for the manufacture of a pharmaceutical composition according to claim 1, whereby

(i) the local anaesthetic(s) and the surfactant with the lowest molecular weight if more than one surfactant is used, are melted together;

(ii) a part of the water is slowly added to the melt (i) during homogenization, forming an emulsion concentrate;

(iii) if more than one surfactant is used, the surfactant with the higher molecular weight is dispersed in water;

(iv) the emulsion concentrate of step (ii) and part of the surfactant solution of step (iii) are thoroughly mixed;

(v) the pH-value is adjusted by the addition of a suitable acid or base;

(vi) the weight is adjusted with water to the final weight of the composition.

Abstract

The invention is directed to a novel pharmaceutical composition comprising one or more local anaesthetics in oil form, one or more surfactants, water and optionally a taste masking agent. The novel composition is advantageously used as a local anaesthetic for pain relief within the oral cavity.

DECLARATION (37 CFR 1.63) AND POWER OF ATTORNEY

As a below-named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name, and

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled NEW PHARMACEUTICAL COMPOSITION WITH ANAESTHETIC EFFECT , Docket No. ABA300/58000 the specification of which

[ ] is attached hereto.

[ ] was filed on as Application No. and was amended on .

[x] was filed on 1 April 1997 as PCT International Application No.PCT/SE97/00566 and was amended under PCT Article 19 on , if applicable.

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the examination of this application in accordance with 37 CFR 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, Section 119, of any foreign application(s) for patent or inventor's certificate or of any PCT International Application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application for patent or inventor's certificate or any PCT International Application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application on which priority is claimed:

Application Serial No.	Country	Filing Date (Day/Month/Year)	Priority Claimed (Yes/No)
9601421-2	Sweden	12 April 1996	yes

I hereby claim the benefit under Title 35, United States Code, Section 120, of any United States application(s) or PCT International Application(s) designating the United States of America that is/are listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application(s) in the manner provided by the first paragraph of Title 35, United States Code, Section 112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, Section 1.56, which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

Application Serial No.	Filing Date	Status (Patented, Pending, Abandoned)

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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